

TAMING THE LIONS: MANAGING VPD OUTBREAKS



Vaccine-Preventable Disease Program
Communicable Disease Branch
North Carolina Division of Public Health

Presentation Outline



- I. Pertussis Basics
- II. Outbreak Investigations
- III. Outbreak of Measles in North Carolina

Pertussis 101



Zack Moore, MD, MPH
Communicable Disease Branch
North Carolina Division of Public Health

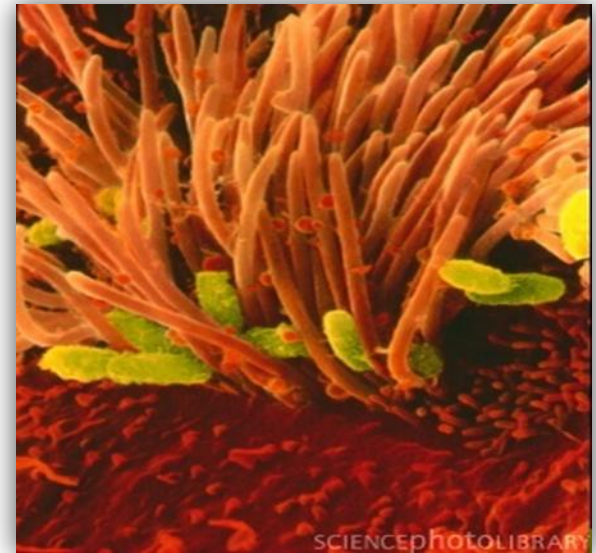
Pertussis

- Highly contagious respiratory infection
- Spread by coughing or sneezing
- >80% susceptible household contacts infected



Bordetella pertussis

- Bacteria that cause pertussis
- Attach to the cilia in upper respiratory tract
- Release toxins, damage cilia and cause inflammation



Stages of Pertussis

Stage	Length	Clinical Features
Catarrhal	1–2 weeks	Runny nose, mild cough
Paroxysmal	1–6 weeks, up to 10	Paroxysmal cough
Convalescent	Weeks to months	Less persistent cough; secondary infection

Images of Pertussis



Source: www.immunize.org, courtesy of Thomas Schlenker, MD, MPH, Chief Medical Officer, Children's Hospital of Wisconsin and the Pennsylvania Chapter of the American Academy of Pediatrics

Infant Pertussis



Source: ShotofPrevention.com. Brady passed away at 2 months from pertussis.

- ❑ Highest risk for complications
- ❑ Atypical symptoms
- ❑ Catarrhal stage and cough minimal or absent
 - ▣ Whoop infrequent
 - ▣ Apnea (sometimes with seizures)
 - ▣ Sneezing
 - ▣ Gagging, choking, vomiting
- ❑ >50% require hospitalization
- ❑ 1% of hospitalized infants die

Adult Pertussis

- Prolonged cough illness
- Wide spectrum of presentation
 - ▣ Classic symptoms to asymptomatic
 - ▣ Persons with mild disease can still transmit infection
- Often undiagnosed



Pertussis in Public Health

- Clinical Case Definition: Cough illness lasting at least 2 weeks with *one* of the following:
 - ▣ Paroxysms of coughing
 - ▣ Inspiratory “whoop”
 - ▣ Post-tussive vomiting

- Laboratory criteria for diagnosis
 - ▣ Positive *B. pertussis* culture or
 - ▣ Positive polymerase chain reaction (PCR)

Pertussis Labs: No Perfect Test

WHAT CLINICIANS WANT

- High sensitivity
(few missed cases)
- Rapid results

WHAT HEALTH DEPARTMENT WANT

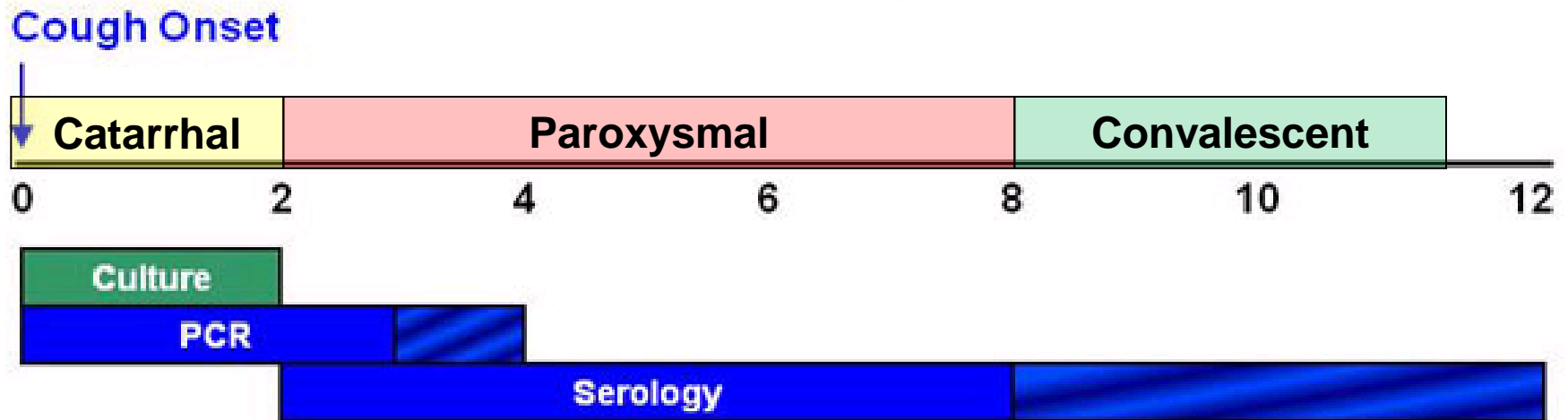
- High specificity
(few false positives)
- Confirm etiology
- Avoid “pseudo-outbreaks”



Pertussis Tests

TEST	PROS	CONS
PCR	<ul style="list-style-type: none">• Sensitive• Fast	<ul style="list-style-type: none">• False positives
Culture	<ul style="list-style-type: none">• Specific (100%)• Gold standard	<ul style="list-style-type: none">• Slow• Low sensitivity
Serology	<ul style="list-style-type: none">• Detect late after onset	<ul style="list-style-type: none">• Not standardized
DFA	<ul style="list-style-type: none">• None (in 2012)	<ul style="list-style-type: none">• Low sensitivity

Optimal Timing for Diagnostic Testing



Perils and Pitfalls of Pertussis PCR

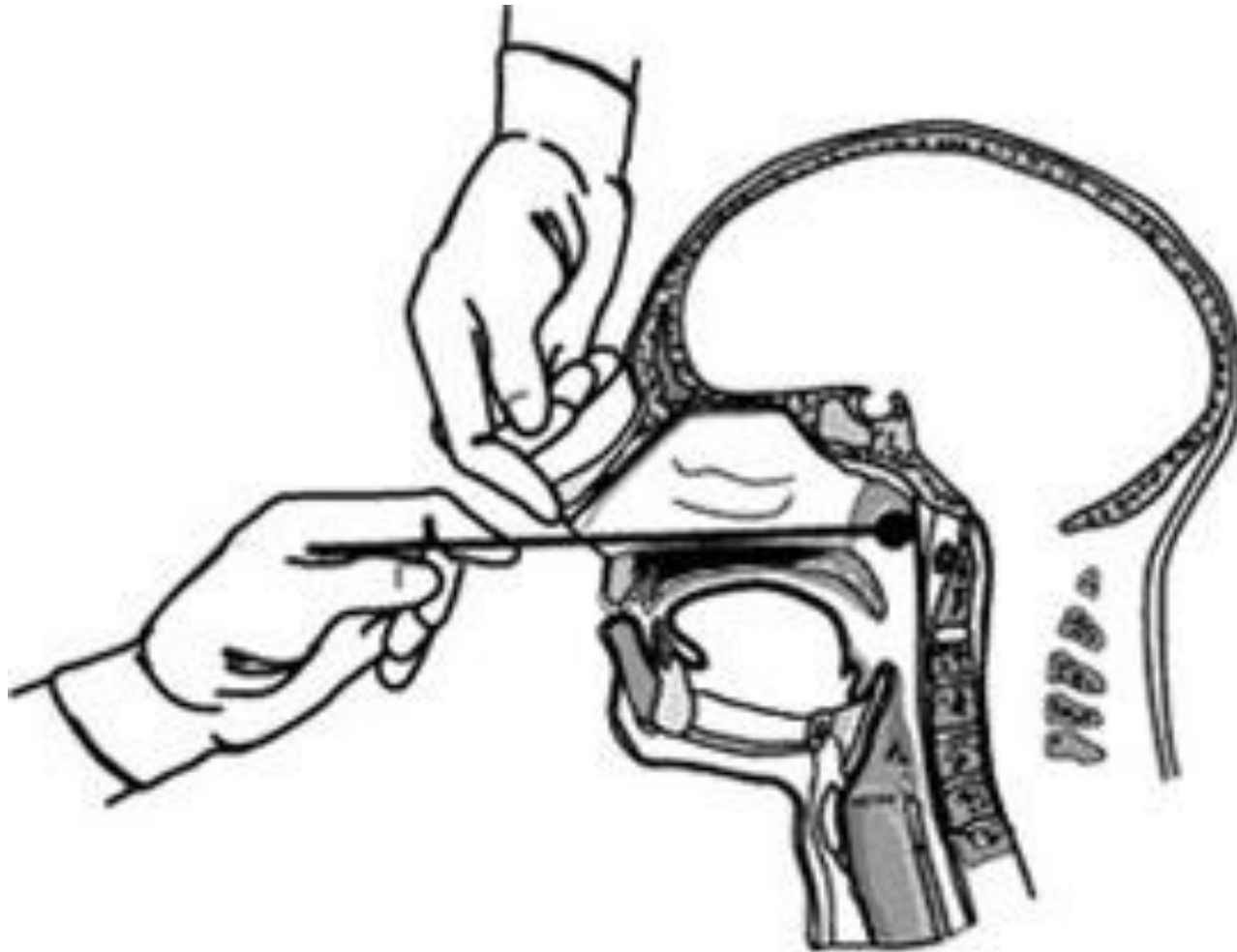
- False positives

- Testing patients without signs/symptoms
- Contamination of swab with vaccine DNA

- False negatives

- Testing too late in illness
- Improper specimen collection

Proper Technique for NP Swab



Pertussis Culture

- High specificity
- Low sensitivity after first two weeks of cough
- Long time to results
- Important for
 - ▣ Control measures in outbreak settings
 - ▣ Antimicrobial resistance testing

The “Pertussis Epidemic that Wasn’t”

Faith in Quick Test Leads to Epidemic That Wasn't

**New York Times, January 22, 2007*

- 134 cases
- No positive cultures
- Confirmatory testing showed no evidence of a pertussis outbreak
- Outbreak of mild respiratory disease with no single etiology

Pertussis Labs: Take Home

- There is no perfect test
 - ▣ Diagnosis based on clinical history and lab results
- PCR should be used *in addition* to culture
 - ▣ Avoid “pseudo-outbreaks”
 - ▣ Appropriate PCR testing
- Limited role for serologies, DFA

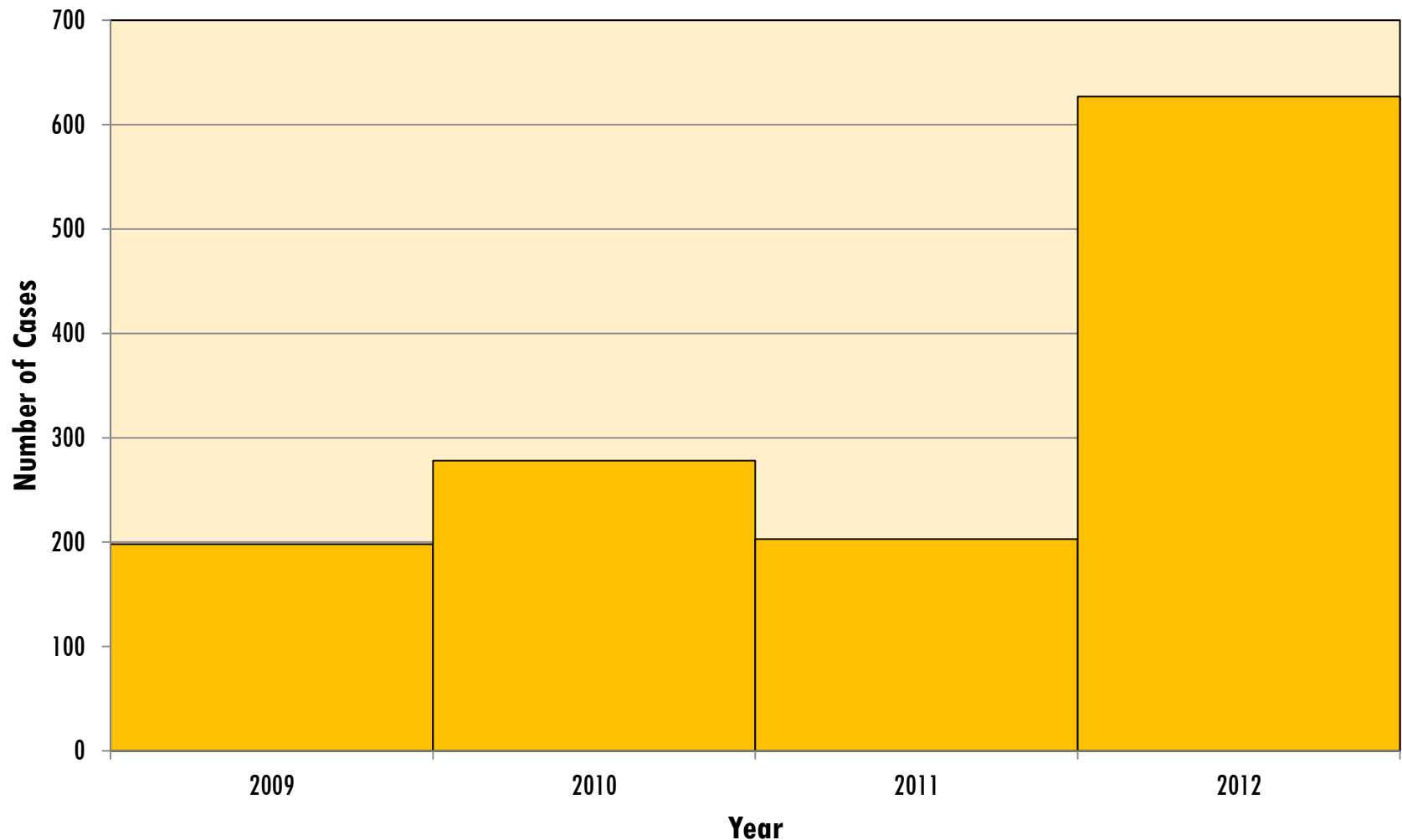
Reported NNDSS pertussis cases: 1922-2012*



*2012 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service

Pertussis Cases Reported in North Carolina, 2009–2012*



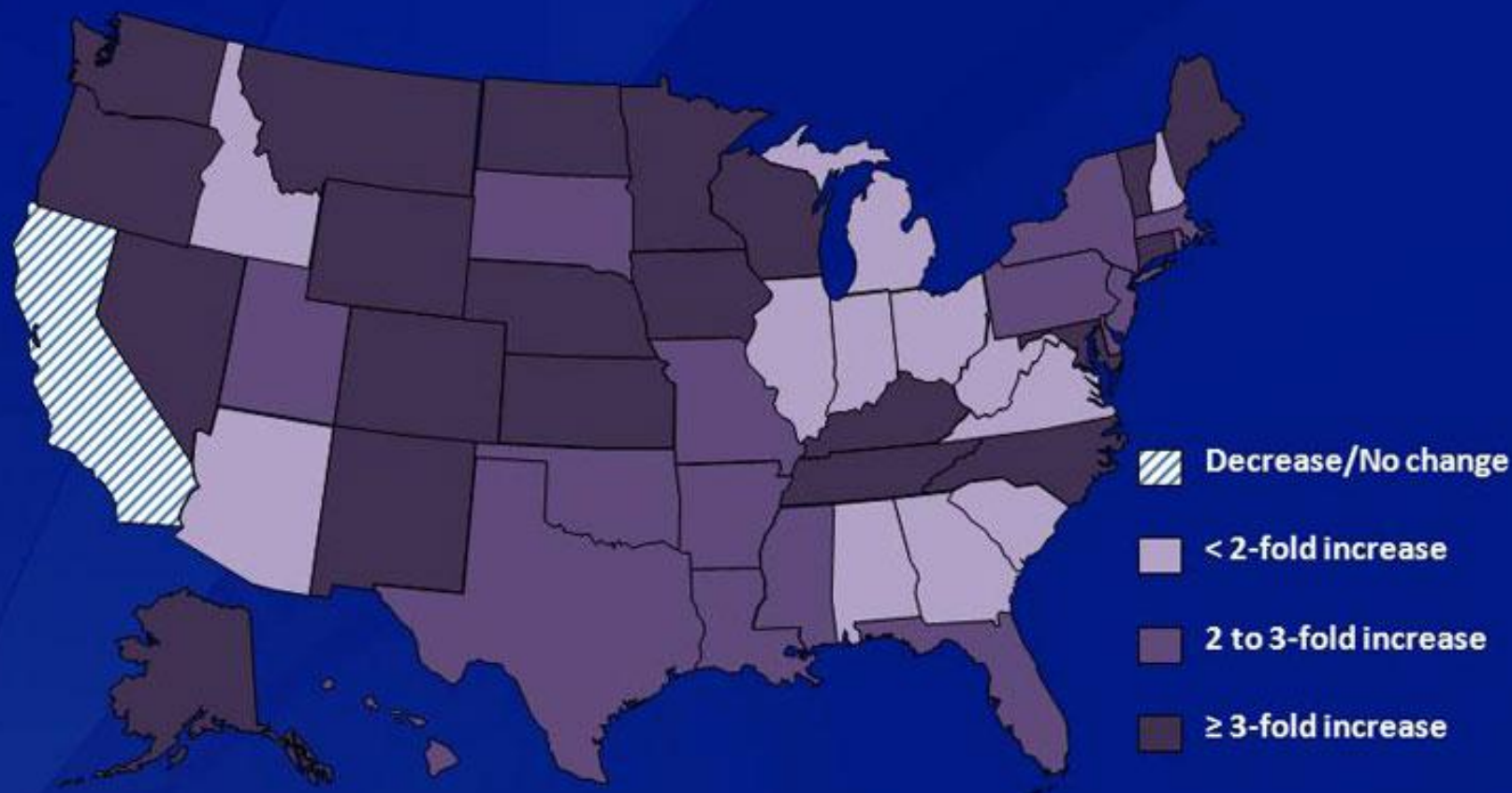
*As of 7/3/13, all data are provisional and subject to change

Pertussis Trends, 2012

- National
 - ▣ 41,880 cases reported
 - ▣ 15 infant deaths
 - ▣ Highest number of cases since 1955
- North Carolina*
 - ▣ 625 cases reported
 - ▣ 20% from Alamance outbreak
 - ▣ 65 counties with cases

*Data are provisional and subject to change

Changes in Pertussis Reporting by State from 2011 to 2012* †

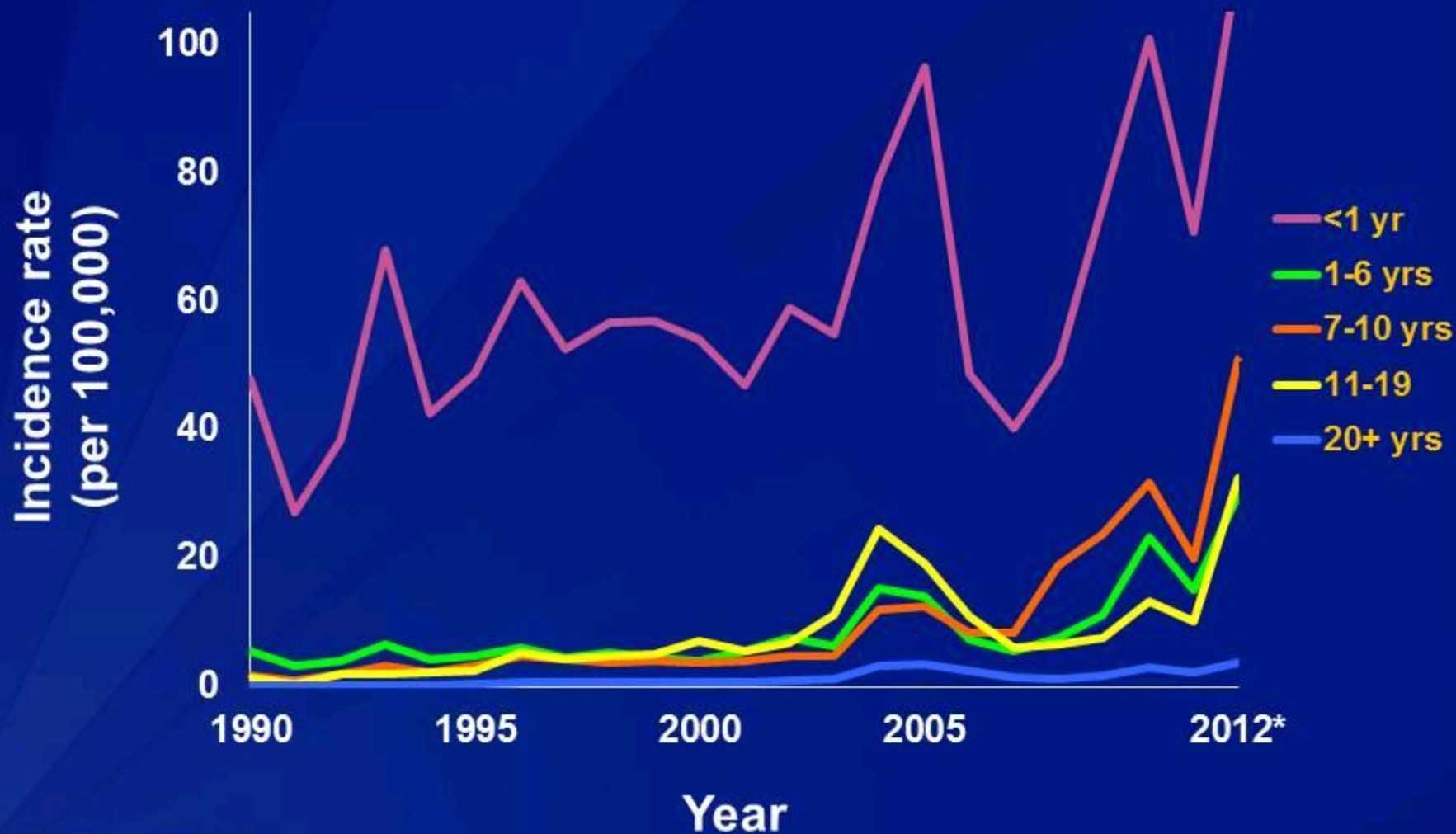


*Data for 2012 are provisional.

†Cases reported through Week 52 in 2011 were compared with cases reported through Week 52 in 2012; fold-changes were calculated for each state.



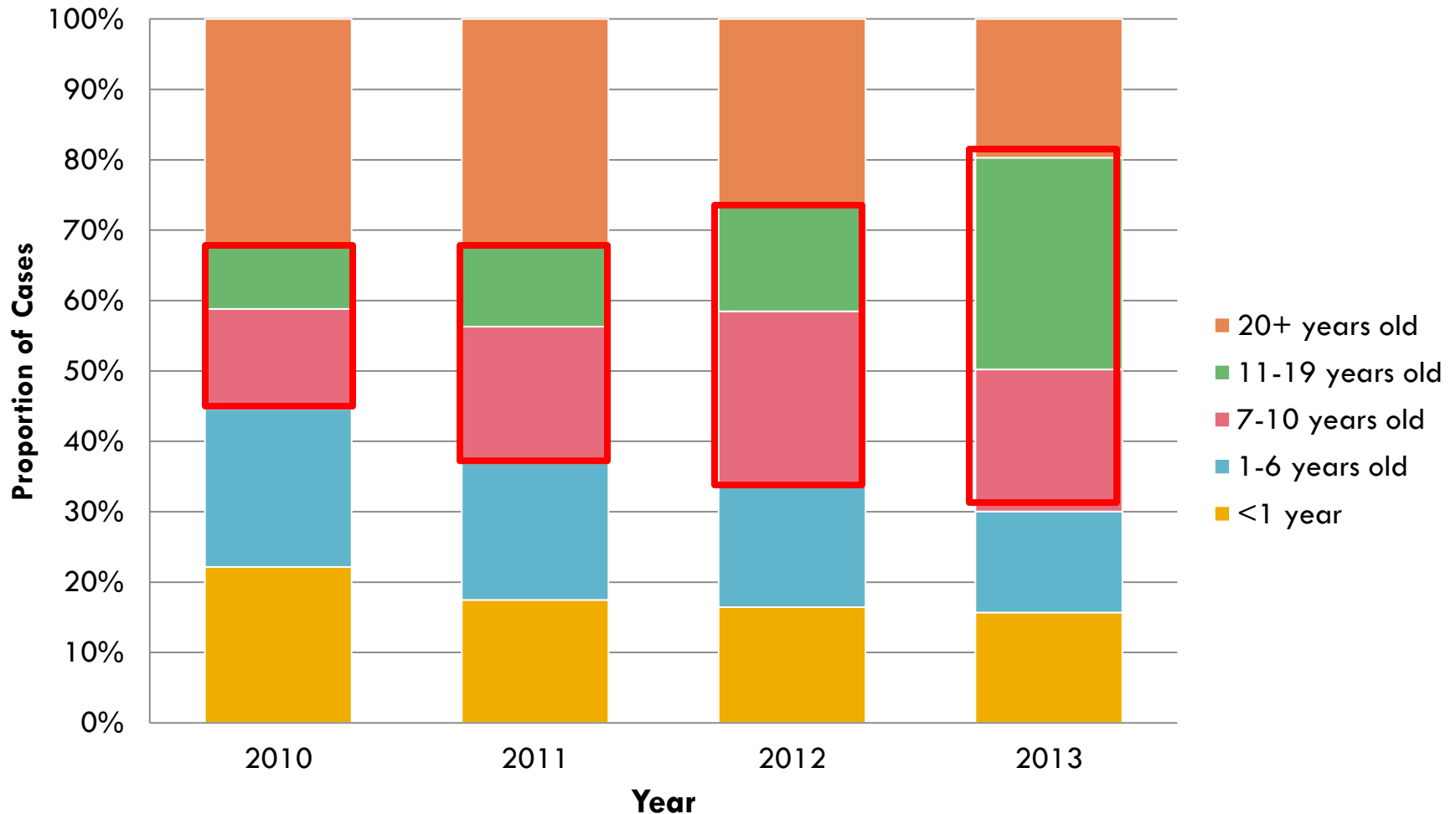
Reported pertussis incidence by age group: 1990-2012*



*2012 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System

Proportion of Pertussis Cases by Age Group, 2010–2013*



*As of 6/28/13. All data are provisional and subject to change.

Reasons for Increase

- Waning immunity from DTaP
- Better diagnostic testing (PCR)
- Increased recognition and reporting
- Natural 3–5 year cycles
- New strains



Pertussis Vaccines

- Most effective way to prevent pertussis
- DTP (1940s) and DTaP (1990s) for infants and children
- Tdap (2005)
 - Children 7–10 who are not fully immunized against pertussis
 - Adolescents 11–18 (preferably at age 11–12)
 - Adults ≥ 19 , especially if in close contact with infants

Waning Immunity



- DTaP and Tdap protection wanes within 5 years
- Likely contributor to increasing incidence, especially among children 7–10
- Highlights need for booster doses

Tdap: Recent Changes

- Recently approved for
 - ▣ Pregnant women
 - ▣ People ≥ 65 years of age
- Expectant mothers should receive Tdap during each pregnancy, preferably at 27–36 weeks

Post-Exposure Prophylaxis (PEP)

- Mainstay of pertussis response
- New recommendations: More limited use
 - ▣ Focus on those at highest risk for severe illness
- Reasons for change:
 - ▣ No data to indicate that widespread use of PEP effectively controls or limits the scope of pertussis outbreaks
 - ▣ Concerns re: overuse of antibiotics

Post-Exposure Prophylaxis (PEP)

- Primary objective: Prevent death and serious complications in individuals at increased risk of severe disease

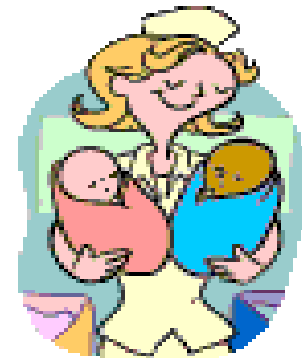


Who Gets PEP?

- All household contacts
- Close contact at high risk for severe illness
 - ▣ Infants, women in 3rd trimester
 - ▣ Those with pre-existing health conditions that may be exacerbated by a pertussis infection
- Close contact who are themselves in close contact with a someone else at high risk for severe illness

Who Gets PEP?

- All contacts in high risk settings that include infants aged <12 months or women in the third trimester of pregnancy
- Examples:
 - ▣ Neonatal intensive care units
 - ▣ Childcare settings
 - ▣ Maternity wards



Broader Use of PEP?



- Consider in situations with
 - ▣ Small number of cases
 - ▣ Limited closed settings
 - ▣ No ongoing, community-wide outbreak
- Consultation with health department

Control Measures

Vaccinate all HCWs with Tdap!



New Solutions?

- Change from broad to targeted prophylaxis
- Improved diagnostic testing options
 - ▣ Broader access to PCR
 - ▣ Increasing attention to standardizing serologic tests
- Changes to vaccine schedule being considered
 - ▣ No current recommendation for Tdap revaccination except in pregnancy

Summary



- Pertussis is an increasing problem
 - ▣ Increasing incidence likely related to shorter duration of immunity since introduction of DTaP
- Vaccination is the best tool for prevention
- Urgent need for new prevention and response strategies



Outbreak Investigations

Vaccine Preventable Diseases



Susan Sullivan RN-BC, MS
Communicable Disease Branch
North Carolina Division of Public Health

'Twas the Week Before Christmas

- ❑ 4pm on Friday: Positive pertussis PCR reported
 - ❑ 8 year-old girl
 - ❑ 2nd grade student at public school
 - ❑ Cough onset before Thanksgiving
 - ❑ Attended school while sick
- ❑ Low suspicion for pertussis when specimen collected
 - ❑ Health department and school not notified
- ❑ Parents say other children coughing in school



Steps of an Outbreak Investigation

1. Identify investigation team and resources
2. Establish existence of an outbreak
3. Verify the diagnosis
4. Construct case definition
5. Case finding: Find cases systematically / develop line list
6. Perform descriptive epidemiology / develop hypotheses
7. Evaluate hypotheses / perform additional studies (as necessary)
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Steps of an Outbreak Investigation

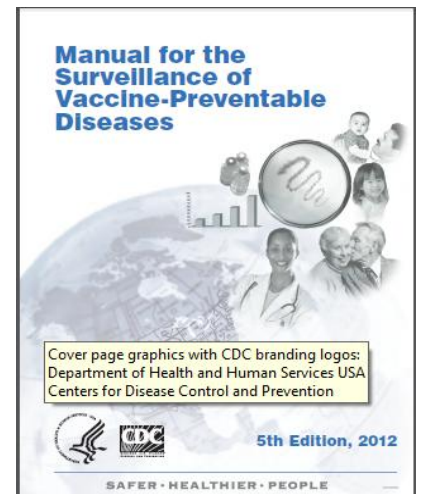
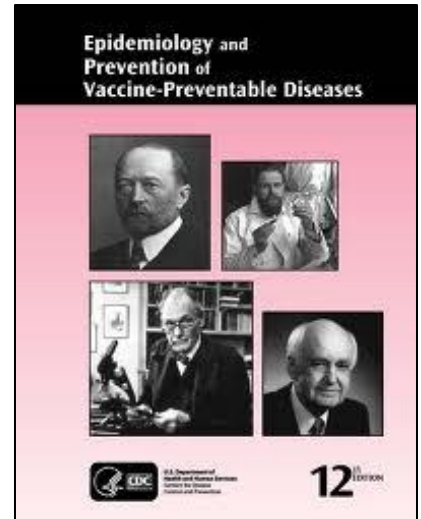
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1. Identify Investigation Team and Resources

1. Identify investigation team and resources
 - a. Identify local and state resources
 - b. Establish investigation team and team lead
 - c. Review information from manuals, scientific literature
 - d. Review authorities for public health actions
 - e. Prepare for field work

Resources for Pertussis Information

- The good:
 - Lots of information
 - ▣ Pink book
 - ▣ VPD manual
 - ▣ CDC pertussis outbreak guide
- The bad:
 - Some information outdated or conflicting
 - ▣ Consult with state VPD staff



Steps of an Outbreak Investigation

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2. Establish Existence of Outbreak

- Pertussis outbreaks can be difficult to identify and manage...so when is it an outbreak?
- It depends...



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R



What is an Outbreak?

- ❑ Five cases of pertussis in one county during December?
- ❑ Two children with varicella in an elementary school?
- ❑ One case of measles?
- ❑ One case of smallpox?

Back to Our Story...

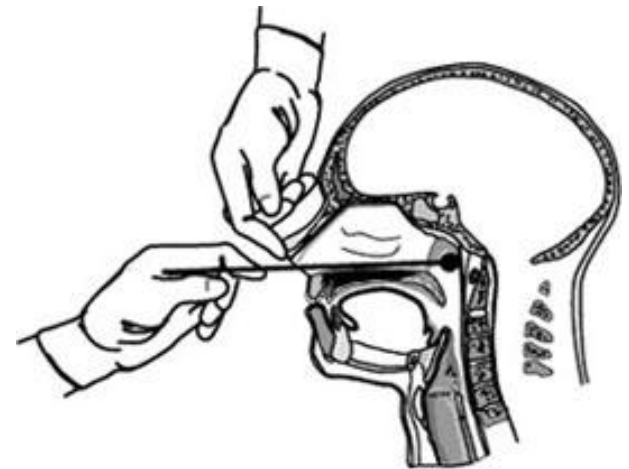
- Convened Epi Team to investigate and respond
- Consulted with state VPD staff, school health, local pediatricians
- Interviewed parents of close contacts from school and bus:
 - ▣ Several other students with cough illness
 - ▣ New suspects identified siblings and other close contacts with classic symptoms of pertussis

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3. Verify the Diagnosis

- Review medical records
- Work with providers to obtain appropriate specimens if needed
- Whenever possible, obtain at least one nasopharyngeal swab for culture, particularly if clinical picture is not clear



Verify the Diagnosis

- Culture already positive in our example
- But what if...
 - ▣ Only serologic results were available?
 - ▣ Children had been coughing <2 weeks?

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4. Construct Case Definition

- Allows uniform way to identify cases
- Standardizes the investigation
- Is specific to each outbreak
 - Person
 - Place
 - Time

Case Definitions vs. Clinical Diagnosis

- Not unusual for clinical diagnosis to differ from surveillance definition, especially in infants
- Clinicians will treat based on clinical findings
- Standardized definitions are for *epidemiologic* purposes and not for treatment

Outbreak Case Definition

- Usually starts broad
- Case definition of ***cough illness lasting 14 days or longer*** has demonstrated 84% sensitivity and 63% specificity for detecting culture-positive pertussis in outbreak settings
- Should be used for epidemiologic investigation and not for reporting purposes



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5. Case finding strategies

- Active surveillance
 - ▣ Interviewing contacts
 - ▣ Surveying class for symptoms
- Passive surveillance
 - ▣ Health alerts
 - ▣ Provider notification
 - ▣ Press release



Line List

- Method to systematically record information
- Simple to review, update, summarize
- Should include basic info
 - ▣ Identifiers (name, date of birth, class, etc.)
 - ▣ Clinical information (symptoms, onset date/time, laboratory results)
 - ▣ Exposure information (links to other cases, etc.)
- Paper (if necessary) or electronic (preferred)

Case Finding Results

- Within School X, you identify:
 - ▣ 4 PCR positive cases
 - 2 also culture-confirmed
 - ▣ 21 epi-linked cases
 - ▣ 20 probable cases

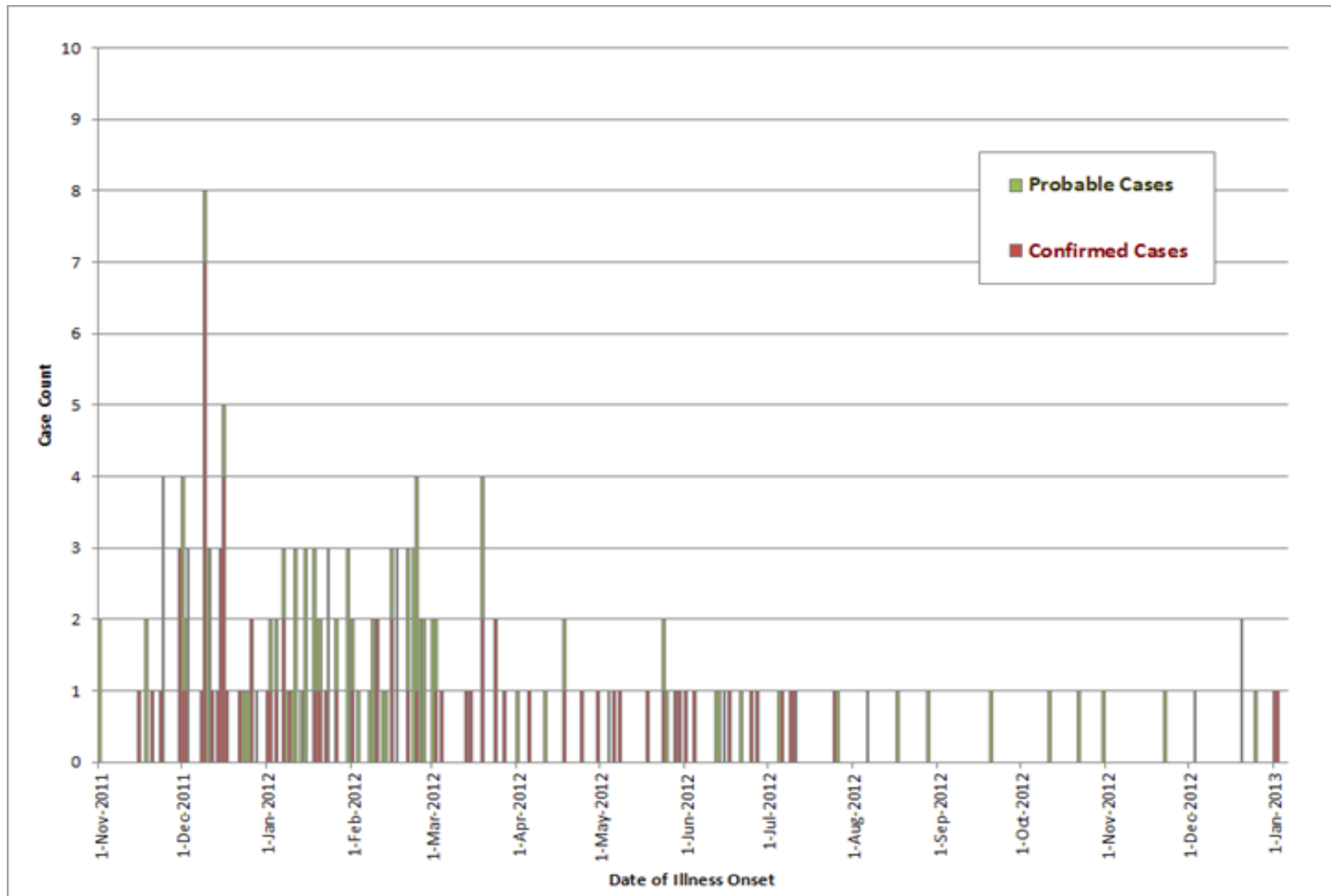
Steps of an Outbreak Investigation

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6. Perform Descriptive Epidemiology

- ☐ Person
 - ☐ Place
- }
- Line List
-
- ☐ Time
- }
- Epidemic curve ('Epi curve')

Confirmed and Probable Pertussis Cases by Date of Cough Onset



Steps of an Outbreak Investigation

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7. **Evaluate hypotheses / perform additional studies (as necessary)**
8. Implement control measures
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7. Evaluate Hypothesis

- Two methods:
 - ▣ Compare hypothesis with established facts
 - ▣ Perform additional studies (e.g., analytic)
 - Cohort or case-control
 - Assess exposures equally among ill and non-ill persons

Pertussis Example: CA 2010

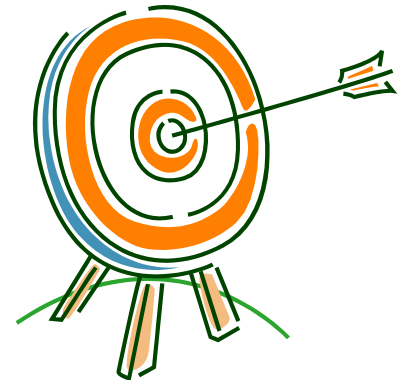
Vaccination Status	Pertussis		OR (95% CI) *
	Case	Control	
Unvaccinated	53	19	8.9 (4.9– 6.1)
5 DTaP doses	629	1,997	

Steps of an Outbreak Investigation

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8. **Implement control measures**
9. Communicate findings
10. Maintain surveillance

8. Implement Control Measures

- Treat cases-when pertussis is strongly suspected, do not wait for lab confirmation
- Identify high risk close contacts during infectious period
 - ▣ Post exposure prophylaxis (PEP)
- Expand access to vaccination
 - ▣ Tdap clinics
- Isolate/exclude ill persons if needed



Goals of Pertussis Control Measures

- Decrease morbidity (amount of disease) and mortality (death) among infants
- Secondary goal is to decrease morbidity among persons of all ages



Steps of an Outbreak Investigation

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9. **Communicate findings**
10. Maintain surveillance

9. Communicate findings

- Maintain ongoing communication during outbreak
 - ▣ Conference calls
 - ▣ Situation reports
 - ▣ Communications with local providers
 - ▣ Periodic public information

- After outbreak
 - ▣ Outbreak summary report
 - ▣ Hot wash (went well, needs work, improvement plan)
 - ▣ After action report (for the response)

Steps of an Outbreak Investigation

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9. Communicate findings
10. **Maintain surveillance**

10. Maintain Surveillance

- Important to
 - ▣ Evaluate / document effectiveness of control measures
 - ▣ Ensure outbreak is over
 - ▣ Ensure secondary outbreak is not occurring
- Maintain surveillance for 2 average incubation periods following the last date of illness onset

Measles Outbreak Associated with a Traveler to India – North Carolina, April–May, 2013



Kristin M. Sullivan, MPH
Communicable Disease Branch
North Carolina Division of Public Health

April 14, 2013

- Report from NC hospital of two suspected measles cases
- Both household contacts of unvaccinated traveler who recently returned from India
- Traveler had experienced similar symptoms
 - ▣ Admitted to hospital
 - ▣ Measles testing not ordered
- Families lived in largely unvaccinated community

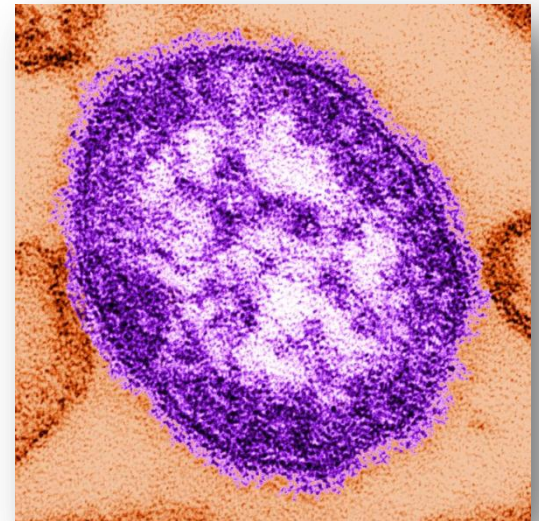
April 16, 2013

- Measles confirmed by lab testing
 - ▣ Positive measles IgM at State Laboratory of Public Health

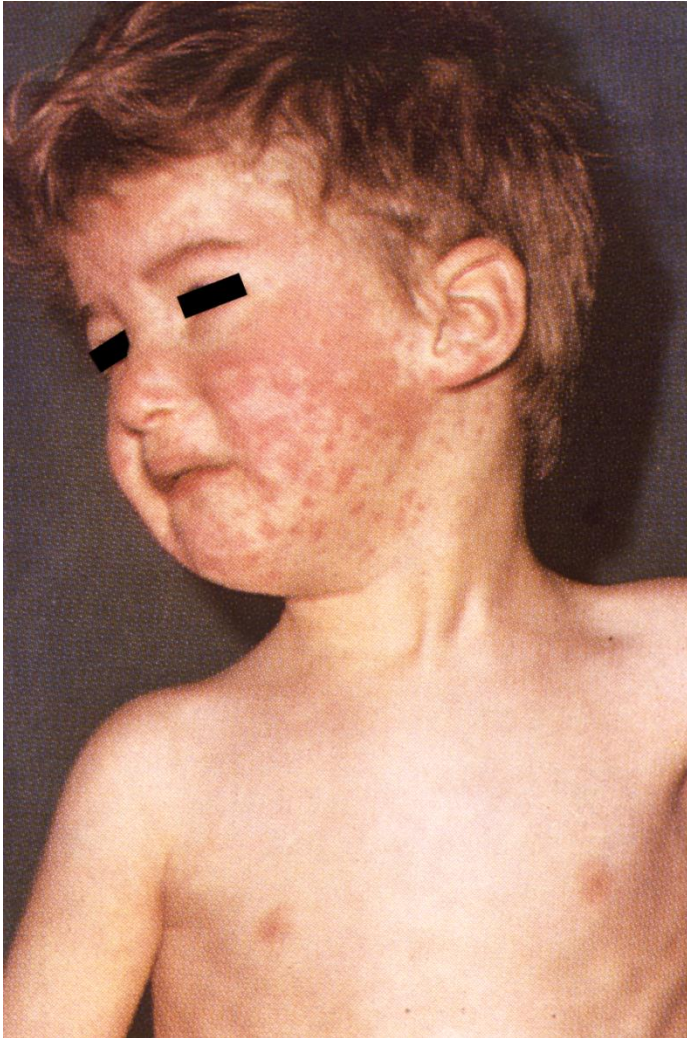


Measles

- Highly contagious viral illness
 - ▣ >90% attack rate among susceptible persons
- Survives <2 hours in air or on surfaces and objects
- Respiratory transmission
- Communicable 4 days before through 4 days after rash onset



Measles Rash

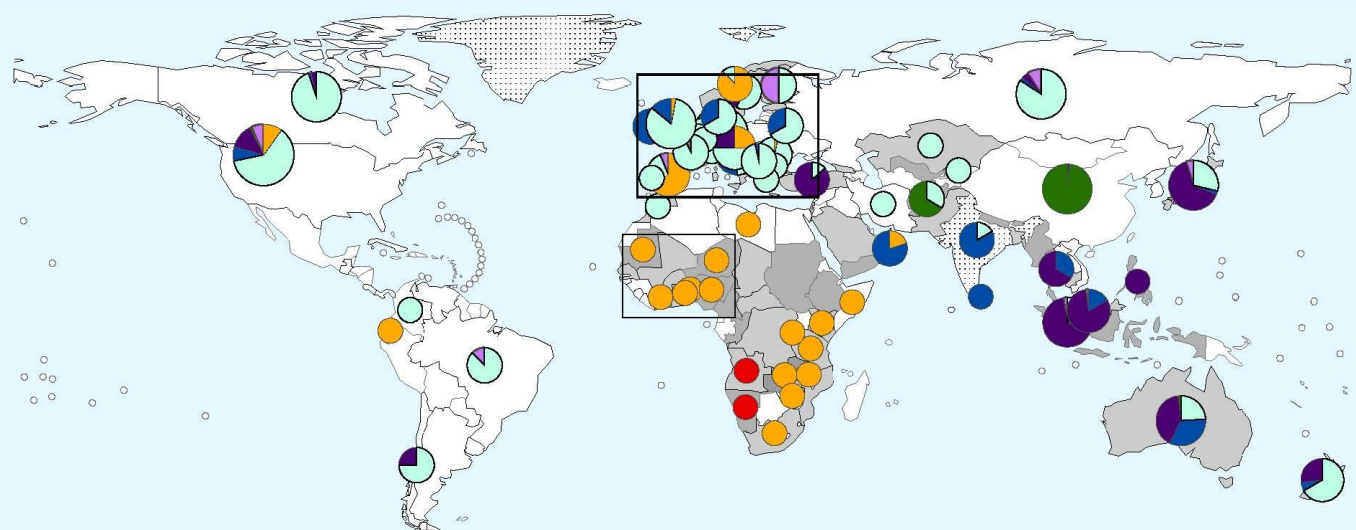


Measles Vaccine

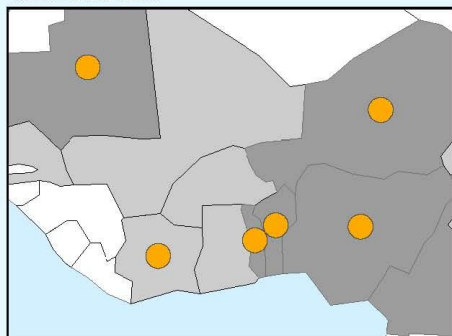
- Vaccine Effectiveness
 - ▣ Primary vaccine failure: 2-5%
 - ▣ ~99% of people receiving 2nd dose respond
- US MMR Vaccination Rates
 - ▣ Children 19-35 months: 92% (2011)
 - ▣ Adolescents ages 13-17 years: 91.1% (2011)

Global View

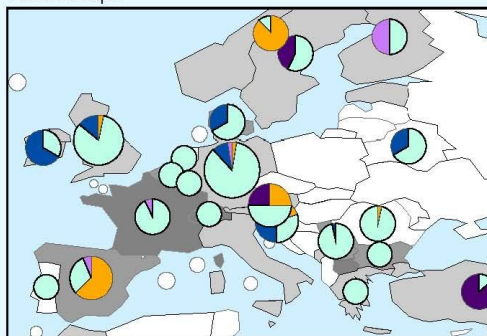
Distribution of measles genotypes, 2011. Data as of 7 December 2011



West Africa inset



West Europe



Genotypes:



**Incidence:
(per 100'000)**

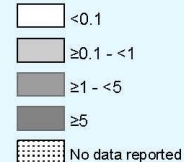


Chart proportional to
number of genotypes



Acknowledgement: WHO Measles LabNet.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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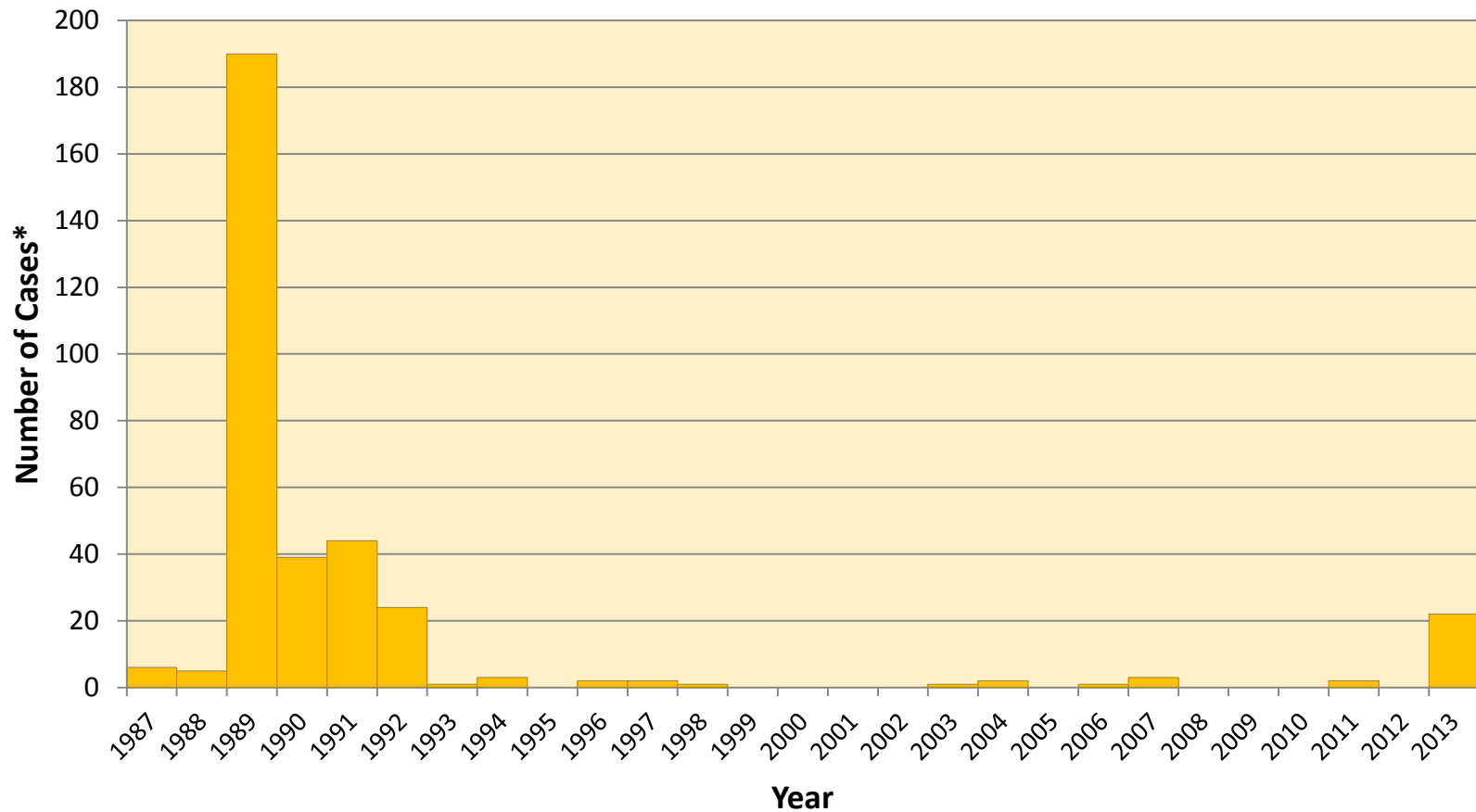
Measles in the United States

- 2000 – eliminated in the United States

Year	Cases
2001-2010	Median: 60 (range: 37–140)
2011	222
2012	54
2013	113 (as of June, 2013)

Measles in North Carolina

**Number of Measles Cases Reported in North Carolina,
1987- June 2013**



*confirmed and probable

Control Strategies

□ Cases

- ▣ Confirm diagnosis
- ▣ Isolate to prevent further spread

□ Contacts

- ▣ Assess for immunity
- ▣ Assess for rash illness
- ▣ Vaccinate or administer immune globulin
- ▣ Quarantine non-immune contacts to prevent further spread

Control Strategies

□ Cases

- ▣ Confirm diagnosis
- ▣ Isolate to prevent further spread

□ Contacts

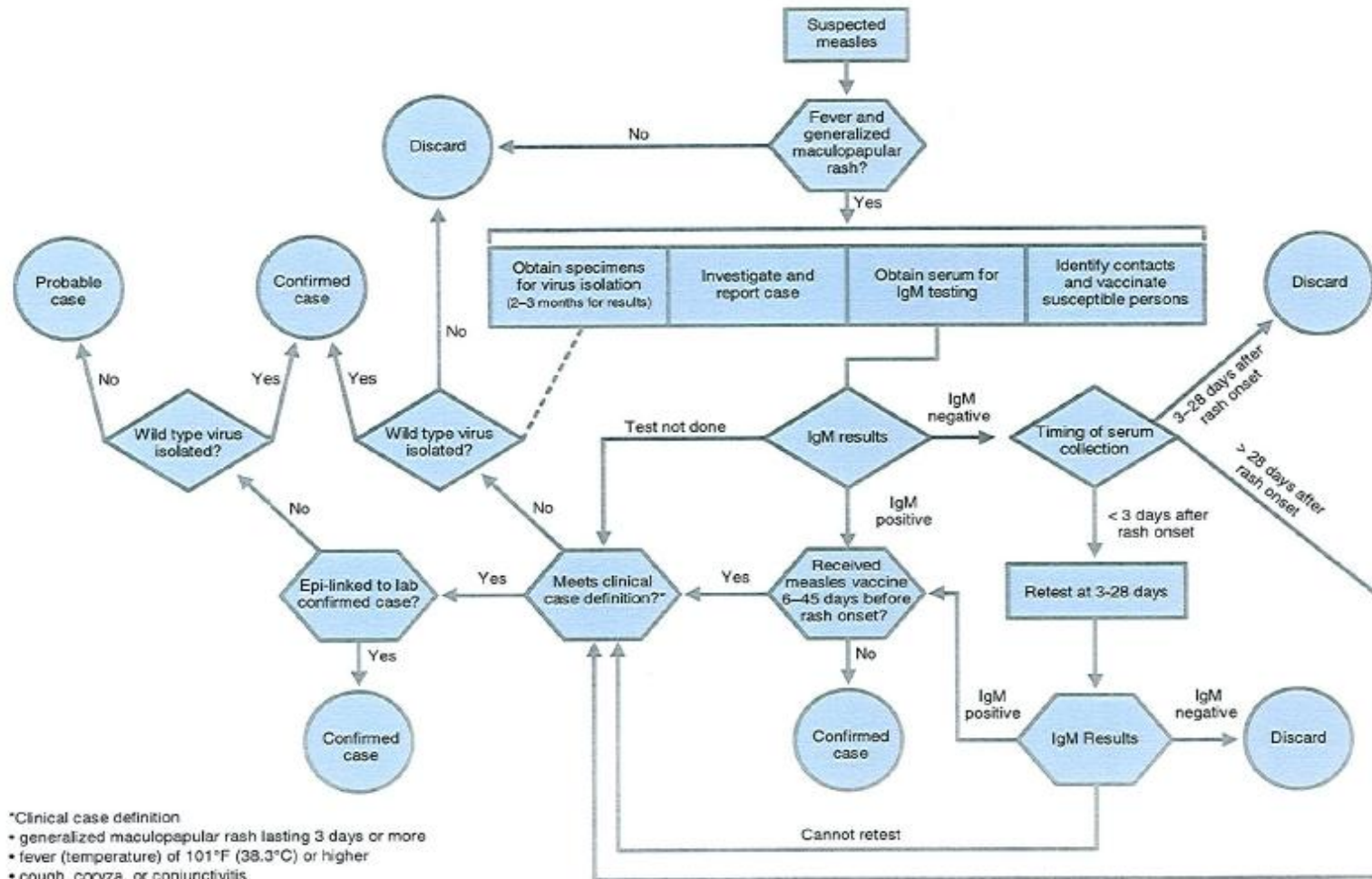
- ▣ Assess for immunity
- ▣ Assess for rash illness
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Suspected Cases:

Confirming the Diagnosis

- Measles IgM (serum)
 - ▣ Rapid result
 - ▣ Requires appropriate timing
 - ▣ Can't distinguish recent vaccination vs. infection
- Viral culture (throat swab or urine)
 - ▣ Slower results
 - ▣ Helps determine source of virus
- PCR
 - ▣ Rapid results
 - ▣ Issues with sensitivity and specificity

Not Always Straightforward...



*Clinical case definition

- generalized maculopapular rash lasting 3 days or more
- fever (temperature) of 101°F (38.3°C) or higher
- cough, coryza, or conjunctivitis

Isolation



- Used for ALL suspected or confirmed cases
- Isolate until 4 days after rash onset

Control Strategies

□ Cases

- Confirm diagnosis
- Isolate to prevent further spread

□ Contacts

- Assess for immunity
- Assess for rash illness
- Vaccinate or administer immune globulin
- Quarantine non-immune contacts to prevent further spread

Who is a contact?

- Shared space for up to 2 hours after case was present
- Shared air supply systems
- Transmission particularly likely in some settings
 - ▣ Households
 - ▣ Schools
 - ▣ Health-care settings
 - ▣ Other institutions (colleges, prisons, etc.).

Contacts: Assess for Immunity

Presumptive Immunity

1. Documentation of adequate vaccination
 - Routine: 1 MMR
 - HCWs: 2 MMR
2. Laboratory evidence of immunity
3. Laboratory confirmation of disease
4. Birth before 1957

Contacts: Assess for Rash Illness

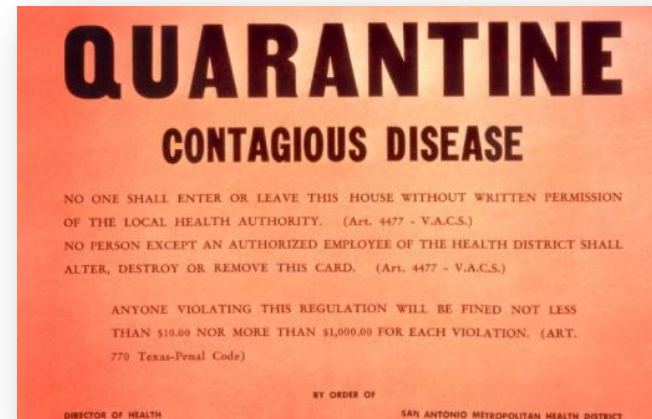
- Prodrome of fever plus cough, coryza, conjunctivitis
- Generalized maculopapular rash
 - Begins on face and head
 - Becomes confluent
 - Persists 5-6 days
- Exposure 7–18 days before rash onset

Contacts: Vaccinate or Administer IG to Susceptibles

- MMR vaccine
 - ▣ Given within 72 hours of exposure
 - ▣ 10% vaccinees will have fever and rash ~10 days after vaccination
- IG
 - ▣ For high-risk contacts
 - ▣ Given within 6 days of exposure

Quarantine

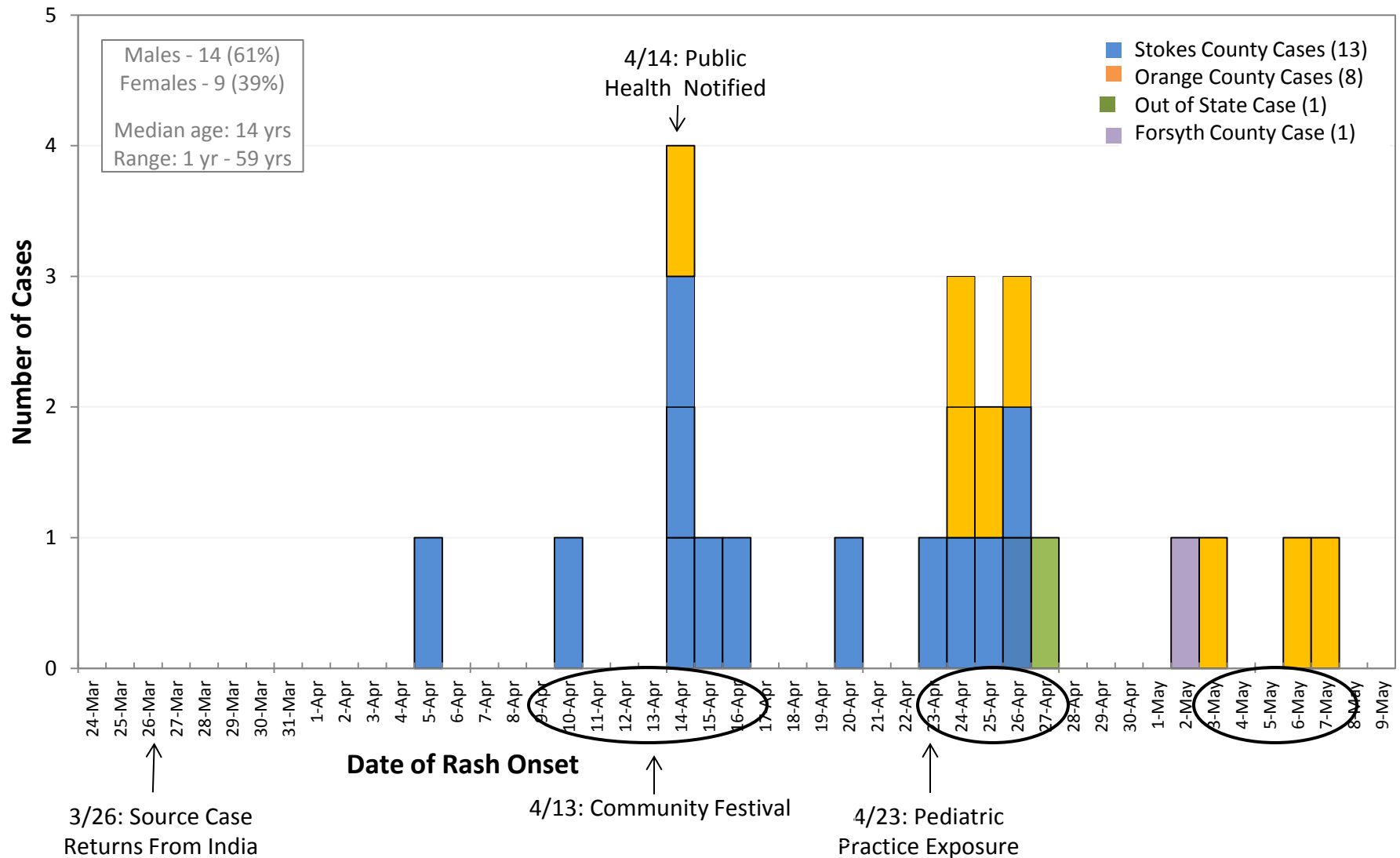
- Used for all non-immune contacts to a suspected or confirmed measles case
- Quarantine from 5th–21st day after exposure
 - ▣ Multiple exposures extend quarantine



Summary of NC Outbreak



Number of Measles Cases by Date of Rash Onset (n=23)



NC Outbreak Response

- 30 isolation orders issued from 5 counties
- 89 quarantine orders issued in 8 counties
- Intensive investigation of large-scale exposures in several venues, including
 - ▣ Hospitals
 - ▣ Physician offices
 - ▣ Festivals / public gatherings

1,000+ contacts
identified and investigated!

MMR/IG Use Related to Outbreak

- 20 counties approved for liberal use
- >1,500 MMR doses administered
- Immune globulin given to 13 high-risk persons

Summary

- One case of measles in an unvaccinated traveler led to 22 additional cases with onsets over a 5 week period
- Outbreak response was resource intensive
 - ▣ Estimated 1,049 contact investigations
 - 465 health care workers
 - ▣ Many state and local health department staff hours
- Communities and clinicians should:
 - ▣ Maintain high immunization rates
 - ▣ Consider measles in unvaccinated travelers

Acknowledgments

- Some slides adapted from Stacey Martin, MSc: “Coughing up the Facts on Pertussis – Emerging Trends and Vaccine Recommendations”, available at <http://www.cdc.gov/vaccines/ed/ciinc/Pertussis.htm>

Questions?



**Not Vaccinated?
No Kisses!**

Get the adult whooping cough vaccine.
www.VaccinateYourFamily.org

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